



Research Paper

Study on anticancer extracts from the fruits of *Lonicera maackii* (Rupr.) Maxim

Accepted 26th February, 2021

ABSTRACT

Lonicera maackii (Rupr.) Maxim is a deciduous shrub which is widely distributed in northern China and has strong adaptability to the dry climate. It is cultivated as an ornamental plant. Some chemical components from the fruits and flowers together with the biological activities have been reported. However, there is no research on material basis of *L. maackii* (Rupr.) Maxim. In addition, the fruits were eaten by birds, whether it can also be consumed by human beings or whether we can find new compounds for development of the new drugs from the fruits? This study was conducted based on these points of view, and we obtained different polar extractions from the fruits of *L. maackii* (Rupr.) Maxim and evaluated their *in vitro* anticancer activity for selecting the potent extraction, and then isolating the potent compounds from the active extraction for development of anticancer agents.

Key words: Fruits of *Lonicera maackii* (Rupr.) Maxim, active extraction, antitumor activity.

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INTRODUCTION

Lonicera maackii (Rupr.) Maxim (which means Amur honeysuckle in English, gold and silver wood in Chinese, Figure 1) is a deciduous shrub of *Lonicera* from Caprifoliaceae, mainly distributed in northeast, north and northwest in China. With the survival advantages of cold resistance, drought resistance, strong resistance to plant disease and insect pests, and easy reproduction, it is often cultivated and reproduced as ornamental plants for beautifying the environment. It was reported that the aqueous extraction of the roots of *L. maackii* exhibited effective activities of anti-inflammatory (Liu et al., 1992), removing fever and improving immune system; the granules can be used to treat pulmonary fever bronchitis in children caused by bacteria (Jiao and Lu, 1986), and it was also used for treatment of the malaria disease (Zhu, 1989). Some chemical components (including iridoids, triterpenes, volatile oils, flavonoids, phenylpropanoids, etc.) in the fruits, flower and leaves of *L. maackii* have been reported (Yang et al., 2018; Gao et al., 2018; Li et al., 2016; Zhu et al., 2017; Yong et al., 2014; Yong et al., 2014), and some biological activities (such as antioxidant activity (Li et al., 2012), antitumor activity (Chai, 2010; Volate et al., 2005), antibacterial activity (Ren et al., 1991), protective liver (Su,

2008; Xie, 2012), reducing blood sugar (Xie, 2012), etc.) have also been reported.

However, there is no report about the research on the material basis of *L. maackii* (Rupr.) Maxim. In this study, we obtained different polar extractions from the fruits of *L. maackii* (Rupr.) Maxim and tested their *in vitro* anticancer activity to select the active extraction, and then, to isolate the active compounds from the active extraction for discovering the new anticancer drugs or drug candidates. The experimental procedures are listed in Figure 2.

EXPERIMENT

Materials and instruments

The fruits of *L. maackii* were collected at the campus of Ningxia Medical University (Ningxia Province of China) in 2019 and aired dried. Other chemicals used for chemical extractions and biological evaluations are analytical reagents and commercially available. The instrument used for these processes was full-wavelength multifunctional microplate reader (Multiskan GO, USA).



Figure 1: The picture of flowers and fruits of *Lonicera maackii*.

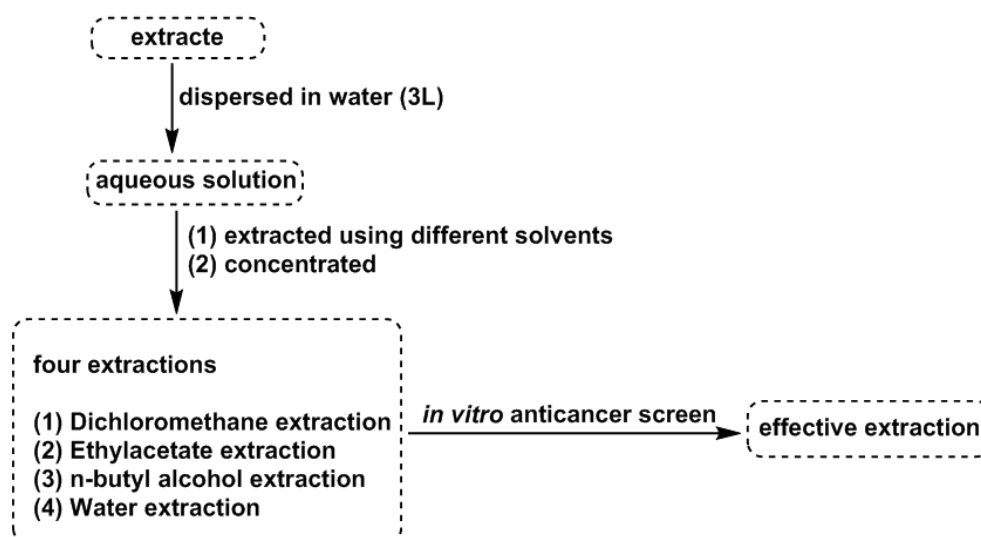


Figure 2: The processes of extraction of the *Lonicera maackii* fruits.

Detailed processes of extraction

3 kg of the crude extract from the fruit of *L. maackii* was dispersed in 3 L deionized water, and extracted with dichloromethane, ethyl acetate and *n*-butyl alcohol (3×3 L), respectively. Four different polar extractions (including water layer) were obtained, which were concentrated under reduced pressure, and then dried in vacuum drying oven at 60°C to obtain the samples for biological screen.

Preliminary *in vitro* anticancer evaluation

The anticancer activity of obtained extractions

(dichloromethane extraction, ethyl acetate extraction, *n*-butyl alcohol extraction and water layer) was evaluated against breast cancer (MCF-7), lung cancer (A549) and Hela cell lines using the counting kit-8 (CCK-8) method (Tominaga et al., 1999). The evaluation processes were described elsewhere with some modifications. Briefly, the four extractions were dissolved in DMSO at a starting concentration of 27.0, 37.2, 31.2 and 28.3 mg/ml respectively for below using.

The procedure for anticancer evaluation

The target cancer cell lines were seeded in 96-well plates

Table 1: The inhibition rate of four extracts on tumor cells.

Extractions	Concentrations (mg/mL)	Inhibition (%)		
		Breast cancer (MCF-7)	Lung cancer (A549)	Hela
DCM	27.0	51.77	92.46	44.90
EA	37.2	20.89	79.00	14.28
<i>n</i> -BuOH	31.2	23.65	59.76	30.77
Water	28.3	19.49	11.13	35.28

(5000 cells/well) with 100 μ l DMEM supplemented with 10% fetal bovine serum, and cultured at 37° C in a humidified CO₂ incubator (95% air, 5% CO₂) for 24 h. While the cell lines grew to 90% in logarithmic growth, the culture medium was removed from each well, and 100 μ l fresh DME was added to each well. Then, 10 μ l above prepared solutions of different extractions were added into each well (every concentration was repeated for 5 times) and the plates were incubated for another 48 h at 37°C. Subsequently, 10 μ l CCK8 was added to each well, and the plates were cultured at 37°C for another 4 hours. The optical density was measured at a wave-length of 450 nm on an ELISA microplate reader. DMEM and DMSO solution (V/V: 10/1) was used as a negative control. The results were expressed as the inhibition calculated at the ratio {[1-(OD₄₅₀ treated/ OD₄₅₀ negative control)] $\times$ 100}. By comparing the anticancer efficacy of four different extractions, dichloromethane extract exhibited higher anticancer efficacy against breast cancer (MCF-7), lung cancer (A549) and Hela cell lines. The results are shown in Table 1.

From Table 1, we can find that the DCM extract exhibited potent anticancer activity against three cancer cell lines at the lowest concentration than that of the other three extractions. Based on this result, we focused on isolating the single compounds from DCM extract for development of anticancer agents.

CONCLUSION AND FUTURE PERSPECTIVES

Our research group over the years have focused on the development of anticancer agents based on the target synthesis and discovery of anticancer agents from the Chinese Traditional Plant Medicines, and so far we have achieved excellent results (Yong et al., 2018; Yong et al., 2018; Yong et al., 2015^a; Yong et al., 2015^b; Yong et al., 2015^c; Lu and Yong, 2015; Lu and Yong, 2016; Yong and Lu, 2017; Yong and Lu, 2019).

Why did we carry out this study? The fruits of *L. maackii* are very rich in north of China, and it can be eaten by birds, but is it nontoxic and can it also be consumed by human beings? and can we discover the new anticancer drugs or drug candidates from the fruits of *L. maackii*? It was based on these points of view, the study was conducted. In this study, we obtained four different polar extractions from the

fruit of *L. maackii* and evaluated their *in vitro* anti cancer efficacy against breast cancer (MCF-7), lung cancer (A549) and Hela cell lines. The results showed that the dichloromethane extraction exhibited higher anticancer activity against the above cancer cell lines, which provided the scientific guidance for the subsequent study. Further studies are being carried out on the isolation of the pure compounds from the DCM extract and screening their anticancer activity for development of anticancer agents.

ACKNOWLEDGEMENTS

This study was financially supported by the National Natural Science Foundation of China (21875252) and Self-created Area Project of Major Science Technology Innovation Platform of Xiamen (3502ZCQ20171002).

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Cite this article as:

Xiao Y, Yong J, Olatunde OZ, Lu Ca (2021). Study on anticancer extracts from the fruits of *Lonicera maackii* (Rupr.) Maxim. *Acad. J. Med. Plants.* 9(5): 066-069.

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